REMARKS

Applicants wish to thank Examiner Winkler for her helpful suggestions regarding claim amendment during her phone conversation with the undersigned on December 11, 2003.

I. Status of the Claims

Claims 1-29 were originally filed and subsequently replaced with claims 1-31. Claim 31 has been withdrawn as the result of a restriction requirement.

Upon entry of the present amendment, claims 28 and 29 are canceled. New claims 32 and 33 are added. Support for claim 32 can be found throughout the specification and in original claim 13. Support for claim 33 can be found in the specification including Example 1 (*e.g.*, page 42, line 12, to page 43, line 12) and original claim 1. Claims 1, 2, 8, 12, 21, 26, and 30 are amended to recite "post-transcriptional regulatory element" before the abbreviation "PRE." Claims 1, 2, 8, 21, 26, and 30 are also amended to recite "human immunodeficiency virus" before the abbreviation "HIV." Claim 2 is further amended to recite "nucleo-cytoplasmic transport element" before the abbreviation "NCTE."

Claims 21-27 are amended to recite an "immunogenic composition," whereas reference to a "vaccine" or "vaccine for the prophylaxis or amelioration of a viral infection in a mammal" is deleted. Claim 26 and 27 are further amended to recite "for eliciting an immune response to a virus in a mammal" in place of "for the prophylaxis or amelioration of a virus infection in a mammal." Support for "eliciting an immune response" can be found in the specification and claim 28 as originally filed. A few other additions and deletions (such as "virus" and "recombinant") are made merely for clarity purpose.

The present amendment adds no new matter.

II. Objections to the Specification

The Examiner objected to the specification for the status of priority patent application and the non-descriptive title. The specification has been amended to address these objections.

III. Objections to the Claims

The Examiner objected to claims 1-30 for using abbreviations without first introducing the full terms. In addition, claim 1 was objected to for having a "(i)" without a "(ii)." The present amendment has addressed these informalities.

IV. Claim Rejections

A. 35 U.S.C. §112 Second Paragraph

Claims 28 and 29 were rejected under 35 U.S.C. §112 second paragraph for allegedly reciting a use without setting forth any steps involved in the process. Since claims 28 and 29 are canceled, this rejection is moot.

B. 35 U.S.C. §112, First Paragraph: Enablement

Claims 21-29 were rejected under 35 U.S.C. §112, first paragraph, for alleged failure to comply with the enablement requirement. Specifically, the Examiner stated that the claimed "vaccine" for the "prophylaxis or amelioration" of a viral infection, particularly HIV infection, is not enabled. Applicants respectfully request the Examiner's reconsideration in light of the present amendment.

As amended, claims 21-27 now recite "immunogenic composition" in place of "vaccine," and the reference to "prophylaxis or amelioration" is deleted. Claims 28 and 29 are canceled. The Examiner has recognized that "just about any protein when inoculated can cause an immune reaction" (the bridging paragraph between pages 4 and 5 of the October 21, 2003, Office Action). Applicants also note that claim 30, which is drawn to a method for eliciting an immune response to a virus in a mammal by administering to the mammal a recombinant virus comprising a PRE, was not rejected on the ground of inadequate enablement. As such, Applicants respectfully submit that amended claims 21-27, drawn to an immunogenic composition comprising a recombinant retrovirus that comprises a PRE, should also be regarded as properly enabled. The withdrawal of the enablement rejection is therefore respectfully requested.

Applicants note that even though the claims are amended to recite "immunogenic composition" in place of "vaccine," an immunogenic composition so defined that may be useful as a vaccine is nonetheless within the claim scope.

C. 35 U.S.C. §112, First Paragraph: Written Description

Claims 2-14 and 16-30 were rejected under 35 U.S.C. §112, first paragraph, for alleged failure to comply with the written description requirement. Specifically, the Examiner pointed to the recitation of at least 80% sequence homology to SEQ ID NO:1 and stated that the specification does not adequately describe the claimed invention by providing commonly shared functional and structural characteristics. Applicants respectfully traverse the rejection.

According to the MPEP, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time the application was filed. Possession of a claimed invention may be demonstrated by description of the invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. MPEP §2163 I. Moreover, a strong presumption exists with regard to originally filed claims that an adequate written description of the claimed invention is present when the application is filed. MPEP §2163 I.A.

Case law indicates that structural features of a claimed invention can be essential to satisfy the written description requirement. The Federal Circuit in *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993), stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d at 1606. The requirement for written description of a chemical genus is further set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406.

On the other hand, proper description of functional features of a claimed invention can also play an important role in satisfying the written description requirement. The Federal Circuit recently stated that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

In the present application, the claimed PRE-containing polynucleotides are defined by shared structural features, *i.e.*, at least 80% sequence identity to SEQ ID NO:1. Percent nucleotide sequence identity of a polynucleotide to a reference sequence is a structural property of the polynucleotide, because such percent identity relies entirely upon the nucleotide sequence of the molecule. Moreover, the recitation of a percentage sequence identity a reference polynucleotide sequence allows one of skill in the art to easily identify the claimed PRE polynucleotides. Algorithms for determining percent sequence identity and sequence similarity for the identification of polynucleotides are well known to those of skill in molecular biology and are described in the present specification, *e.g.*, on pages 23 to 24.

The claimed PRE-containing polynucleotides are also defined by shared functional features, *i.e.*, when inserted in a recombinant, hybrid HIV-1 lacking or having a non-functional wild-type post-transcriptional RNA NCTE, the PRE is capable of functioning as a NCTE in the hybrid HIV-1 to increase the expression of viral proteins such as $p24^{gag}$; and when the PRE-containing hybrid HIV-1 virus infects activated human peripheral blood mononuclear cells (huPBMCs), the level of expression of HIV-1 $p24^{gag}$ is between about 5 fold and about 200 fold less than levels of $p24^{gag}$ expression when HIV-1 wild type virus, utilizing wild-type NCTE, infects activated huPBMCs. Functional assays for identifying the claimed PRE polynucleotides are known in the art and also provided by the specification. On page 25, lines 2-31, for instance, the specification teaches methods for measuring expression levels of viral proteins such as HIV-1 $p24^{gag}$. These assays thus allow one skilled in the art to readily identify the claimed PRE-containing polynucleotides based on the PRE's functional features.

The present invention relates to the discovery of a post-transcriptional regulatory element (PRE). It is Applicants' intent to include in the claim scope nucleic acids containing allelic variants and man-made mutants that retain or enhance the PRE's normal function (*see, e.g.*, page 26, lines 2-7 of the specification). For example, the specification describes an exemplary PRE sequence of 231 nucleotides, SEQ ID NO:1, on page 44. A second exemplary PRE sequence of 226 nucleotides, SEQ ID NO:5, is disclosed on page 45. According to the specification, SEQ ID NO:1 and SEQ ID NO:5 are nearly identical except that SEQ ID NO:1 has 2 fewer nucleotides at the 5' end and 7 additional nucleotides at the 3' end.

More importantly, the specification further teaches a third exemplary PRE sequence, SEQ ID NO:6, which has about 83% sequence identity to SEQ ID NO:1 and is set forth in the bridging paragraph between pages 46 and 47. An artisan can compare the sequences of the most diverse variants, *e.g.*, SEQ ID NO:1 and SEQ ID NO:6, and recognize the critical region(s) where the nucleotide sequence must remain unaltered in order to preserve the desired functions of PRE as well as the non-critical region(s) where modification of nucleotide sequence has no or little effect on functionality. These PRE sequence variants thus provide not only a starting point but also a road map for one of skill in the art to readily generate other functional PRE variants that have a sequence identity greater than 83% but less than 100% to SEQ ID NO:1.

In light of the disclosure of these exemplary PRE sequences, especially SEQ ID NO:6, which has about 83% (*i.e.*, over 80%) polynucleotide sequence identity to SEQ ID NO:1, an ordinarily skilled artisan would reasonably conclude, upon reading the present application, that the inventors had in their possession the claimed invention at the time this application was filed.

In summary, both structural and functional features commonly shared by all members of the claimed genus of PRE polynucleotides have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). This description of the claimed invention is consistent with the standard set forth in *Lilly* and *Amgen*.

As such, Applicants believe that the written description rejection under 35 U.S.C. §112 is improper and should be withdrawn.

D. 35 U.S.C. §102

Claim 1 was rejected under 35 U.S.C. §102(a) for alleged anticipation by GenBank Accession No. C80740 or C80177. This rejection is respectfully traversed.

As established by the Declaration pursuant to 37 C.F.R. §1.131 by inventors Dr. Pavlakis and Dr. Nappi, as well as the evidence submitted therewith, the present inventors had in their possession SEQ ID NO:1 prior to October 20, 1997, which is the earliest entry date for GenBank Accession Nos. C80740 and C80177. Therefore, these two GenBank entries are not available as §102(a) references against the pending claims in the present application. Applicants respectfully request that the Examiner withdraw the anticipation rejection on this ground.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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